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10/570,125	10/23/2006	Albert J. Banes	4647-060533	7408

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
11/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,125	BANES ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,13,14,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13,14,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed August 24, 2009.

Claims 8-12 and 15-18 have been canceled. New claims 19 and 20 are acknowledged. Claims 1-7, 13, and 14 have been amended.

Claims 1-7, 13, 14, 19, and 20 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Nucleotide Sequence Disclosures

In the previous Office Action mailed February 24, 2009, it was noted that this application failed to comply with the requirements of 37 C.F.R. §1.821-1.825. Applicant's Amendment filed August 24, 2009 amending Table 1 of the specification to include sequence identifiers is acknowledged. It is noted that the instant application fully complies with the requirements of 37 C.F.R. §1.821-1.825.

Claim Rejections - 35 USC § 112

In the previous Office Action mailed February 24, 2009, claims 4, 7, and 14 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is withdrawn** in view of Applicant's Amendment filed August 24, 2009. Specifically, the Examiner is withdrawing this rejection in view of

Applicant's Amendment to the claims to remove trademarks from claims 4 and 7. The Examiner is also withdrawing this rejection in view of Applicant's Amendment to claim 14 to correct the typographical error from TGF-α to TNF-α.

Claim Rejections - 35 USC § 102

In the previous Office Action mailed February 24, 2009, claims 1, 13, and 14 were rejected under 35 U.S.C. 102(b) as being anticipated by Hartwig et al. (J Interferon Cytokine Res., 2001 Oct; 21(10):851-860). **This rejection is withdrawn** in view of Applicant's Amendment filed August 24, 2009. Specifically, the Examiner is withdrawing this rejection in view of Applicant's Amendment to the claims to recite that a cytokine, which modulates an organization of a cytoskeleton of the cell and resets the intrinsic strain of the cell is administered. It is noted that Hartwig et al. do not administer a cytokine to cells.

In the previous Office Action mailed February 24, 2009, claims 1, 6, and 7 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,472,202, B1 (Banes et al.), presented and made of record on Applicant's Information Disclosure Statement filed July 19, 2007. **This rejection is withdrawn** in view of Applicant's Amendment filed August 24, 2009. Specifically, the Examiner is withdrawing this rejection in view of Applicant's Amendment to the claims to recite that a cytokine, which modulates an organization of a cytoskeleton of the cell and resets the intrinsic strain of

the cell is administered. It is noted that Banes et al. do not administer a cytokine to cells.

In the previous Office Action mailed February 24, 2009, claims 1-5 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,912,234 A (Ruoslahti et al.), presented and made of record on Applicant's Information Disclosure Statement filed July 19, 2007. **This rejection is withdrawn** in view of Applicant's Amendment filed August 24, 2009. Specifically, the Examiner is withdrawing this rejection in view of Applicant's Amendment to the claims to recite that a cytokine, which modulates an organization of a cytoskeleton of the cell and resets the intrinsic strain of the cell is administered. It is noted that Ruoslahti et al. do not administer a cytokine to cells.

Applicant's Amendment filed August 24, 2009 necessitated the new grounds of rejection(s) presented below:

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 13, 14, 19, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 3, 27, 28, 30, and 31 of copending Application No. 11/076,425 (U.S. Patent Publication No.20060134779). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application are fully encompassed within the claims of the current application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 13, 14, 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Berk et al. (Journal of Biological Chemistry, 1991 Vol. 266:3192-3197).

Claim 1 is drawn to a method for manipulating an intrinsic strain of a cell, comprising culturing the cell on a surface or in a medium, thereby forming a cultured cell; and administering to the cultured cells *in vivo* or *in vitro* a compound that resets the intrinsic strain of the cell in order to modulate extracellular matrix synthesis, secretion, stiffness, organization and/or remodeling, or attachment of the cells to the matrix via integrins or other like cell-matrix attachments, wherein the compound is a cytokine that adjusts the intrinsic strain of the cell by modulating a cytoskeletal gene. Claims 13, 14, 19, and 20 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the cytoskeletal protein is selected from actin, myosin, α-actinin, vimentin, vinculin, and titin matrix metalloproteinases; wherein the cytokine is IL-1β; and wherein the cytoskeletal gene is a gene that expresses or regulates the expression of elastin.

Berk et al. disclose that the expression of elastin and collagen can be regulated by IL-1β in myofibroblasts and lung fibroblasts.

While Berk et al. is silent with respect to manipulating an intrinsic strain of a cell, the method steps carried out by Berk et al. are the same as those recited in the claimed invention (treating of cells with a compound (e.g. cytokine) that affects intrinsic cell strain). Because the method steps are the same, Berk et al. is inherently teaching the same method of manipulating intrinsic strain of a cell as the current application, absent evidence to the contrary.

Claims 1, 13, 14, 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Mauviel et al. (Journal of Biological Chemistry, 1993 Vol. 268:6520-6524).

The claims are as described above.

Mauviel et al. disclose that the expression of elastin and collagen can be regulated by IL-1β in dermal fibroblasts.

While Mauviel et al. is silent with respect to manipulating an intrinsic strain of a cell, the method steps carried out by Mauviel et al. are the same as those recited in the claimed invention (treating of cells with a compound (e.g. cytokine) that affects intrinsic cell strain). Because the method steps are the same, Mauviel et al. is inherently teaching the same method of manipulating intrinsic strain of a cell as the current application, absent evidence to the contrary.

Claims 1, 6, 13, 14, 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Archambault et al. (Journal of Orthopaedic Research, 2002, Vol. 20:36-39).

Claims 1, 13, 14, 19, and 20 are as described above. Claim 6 is dependent on claim 1 and includes all the limitations of claim 1 with the further limitation further comprising applying a mechanical external strain to the cell.

Archambault et al. disclose IL-1β treatment increases the secretion and expression of metalloproteinases in tenocytes. Archambault et al. also disclose applying mechanical cyclic strain to the cell in the form of a stretching protocol with elongation.

While Archambault et al. is silent with respect to manipulating an intrinsic strain of a cell, the method steps carried out by Archambault et al. are the same as those recited in the claimed invention (treating of cells with a compound (e.g. cytokine) that affects intrinsic cell strain). Because the method steps are the same, Archambault et al. is inherently teaching the same method of manipulating intrinsic strain of a cell as the current application, absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7, 13, 14, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archambault et al. (Journal of Orthopaedic Research, 2002, Vol. 20:36-39) in view of U.S. Patent No. 6,472,202, B1 (Banes et al.), presented and made of record on Applicant's Information Disclosure Statement filed July 19, 2007.

Claim 1 is drawn to a method for manipulating an intrinsic strain of a cell, comprising culturing the cell on a surface or in a medium, thereby forming a cultured cell; and administering to the cultured cells *in vivo* or *in vitro* a compound that resets the intrinsic strain of the cell in order to modulate extracellular matrix synthesis, secretion, stiffness, organization and/or remodeling, or attachment of the cells to the matrix via integrins or other like cell-matrix attachments, wherein the compound is a cytokine that adjusts the intrinsic strain of the cell by modulating a cytoskeletal gene. Claims 2-7, 13, 14, 19, and 20 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the cell comprises an *in situ* native tissue; wherein the cell comprises an *in vitro* fabricated tissue engineered construct; wherein the tissue engineered construct is a human tendon fibroblast populated bioartificial tendon or other fibroblast from another connective tissue; wherein the compound is added during or after tissue engineered construct is fabricated; further comprising applying a mechanical external strain to the cell; wherein the mechanical strain comprises uniaxially loading a tissue engineered construct by placing loading posts beneath a well of a culture plate and applying a vacuum to deform a flexible membrane downward so as to apply a uniaxial strain along a long axis of the tissue engineered construct; wherein the cytoskeletal protein is selected from actin, myosin, α-actinin, vimentin, vinculin, and titin matrix metalloproteinases; wherein the cytokine is IL-1β; and wherein the cytoskeletal gene is a gene that expresses or regulates the expression of elastin.

Determining the scope and contents of the prior art

Archambault et al. teach IL-1β treatment increases the secretion and expression of metalloproteinases in tenocytes. Archambault et al. also teach applying mechanical cyclic strain to the cell in the form of a stretching protocol with elongation.

While Archambault et al. is silent with respect to manipulating an intrinsic strain of a cell, the method steps carried out by Archambault et al. are the same as those recited in the claimed invention (treating of cells with a compound (e.g. cytokine) that affects intrinsic cell strain). Because the method steps are the same, Archambault et al. is inherently teaching the same method of manipulating intrinsic strain of a cell as the current application, absent evidence to the contrary.

Ascertaining the differences between the prior art and the claims at issue

Archambault et al. do not teach wherein the cell comprises an *in situ* native tissue or an *in vitro* fabricated tissue engineered construct. Archambault et al. also do not teach wherein the mechanical strain comprises a uniaxial strain along the tissue engineered construct.

Banes teaches a loading station assembly and a method for tissue engineering that allows equibiaxial, uniaxial or other directional stretching of a flexible cell culture membrane (see column 2 line 26, and claim 7). The use of a circular loading post (see column 2 line 51) for application of the mechanical external strain with application of a vacuum is also taught (see Abstract).

Banes et al. teach a method for tissue engineering. Banes et al. also teach tissue engineered tendon constructs. Banes et al. explicitly teach that their invention is:

> "Useful for populating a three-dimensional material with tendon or other like cells which can then act as a tendon connective tissue mimetic, for example, in humans, in a tissue engineering

> application. Similarly, other types of cells may be used for other types of mimetics"

Applicant is reminded that with the decision in KSR International v. Teleflex Inc. (82 USPQ2d 1385) it was established that, "Prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art." Given the teachings of Banes et al. one of ordinary skill in the art would understand that "other types of cells" and "mimetics" include *in situ* native tissue and *in vitro* fabricated tissue as recited in claims 2 and 3 of Applicant's invention.

Resolving the level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is considered to be high, being a graduate student or post-doctoral fellow in a biological science.

Considering objective evidence present in the application indicating obviousness or nonobviousness

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made to devise a method for manipulating an intrinsic strain of a cell, comprising culturing the cell on a surface or in a medium, thereby forming a cultured cell; and administering to the cultured cells *in vivo* or *in vitro* a compound that resets the intrinsic strain of the cell in order to modulate extracellular matrix synthesis, secretion, stiffness, organization and/or remodeling, or attachment of the cells to the matrix via integrins or other like cell-matrix attachments, wherein the compound is a cytokine that adjusts the intrinsic strain of the cell by modulating a cytoskeletal gene using the teachings of Archambault et al.

It would have been *prima facie* obvious to one of ordinary skill in the art to have the cell be a tissue engineered construct using the teachings and motivation of Banes et

al. It would have been *prima facie* obvious to one of ordinary skill in the art to further comprise applying a mechanical external strain to the cell using the teachings and motivation of Banes et al. It would have been *prima facie* obvious to one of ordinary skill in the art to fabricate the tissue using the teachings and motivation of Banes et al.

One of ordinary skill in the art would have been motivated to devise a method for manipulating an intrinsic strain of a cell, comprising culturing the cell on a surface or in a medium, thereby forming a cultured cell; and administering to the cultured cells *in vivo* or *in vitro* a compound that resets the intrinsic strain of the cell in order to modulate extracellular matrix synthesis, secretion, stiffness, organization and/or remodeling, or attachment of the cells to the matrix via integrins or other like cell-matrix attachments, wherein the compound is a cytokine that adjusts the intrinsic strain of the cell by modulating a cytoskeletal gene since Archambault et al. taught that such a method can initiate a matrix destructive pathway in a tendon.

One of ordinary skill in the art would have been motivated to further comprise applying a mechanical external strain to the cell since Banes et al. taught that such a method could study the maintenance and integrity of the tendon. One of ordinary skill in the art would have been motivated to fabricate the tissue so that it would have the structural characteristics of host tissue which has been permanently altered by injury.

One of ordinary skill in the art would have had a reasonable expectation of success of devising a method for manipulating an intrinsic strain of a cell, comprising culturing the cell on a surface or in a medium, thereby forming a cultured cell; and administering to the cultured cells *in vivo* or *in vitro* a compound that resets the intrinsic

strain of the cell in order to modulate extracellular matrix synthesis, secretion, stiffness, organization and/or remodeling, or attachment of the cells to the matrix via integrins or other like cell-matrix attachments, wherein the compound is a cytokine that adjusts the intrinsic strain of the cell by modulating a cytoskeletal gene since Archambault et al. taught the successful use and design of such a method for initiating a matrix destructive pathway in a tendon. One of ordinary skill in the art would have had a reasonable expectation of success of applying a mechanical external strain to the cell since Banes et al. taught how to successfully apply mechanical external strain to tendons.

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore can be reached on 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the

number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

November 17, 2009
/Terra Cotta Gibbs/

/Sean R McGarry/
Primary Examiner, Art Unit 1635